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| EXAMINER | |
|---|---|
| SHAHNAN SHAH, KHATOL S | |
| **ART UNIT** | **PAPER NUMBER** |
| 1645 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/524,198 | NUIJTEN | |
| | Examiner | Art Unit | |
| | Khatol S. Shahnan-Shah | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-10 and 13-20* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 13-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 -9* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 February 2005* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

**1.** Applicants' response to restriction requirement of 7/20/2007 is acknowledged.

### *Status of Claims*

**2.** Claims 1-10 and 13-20 are pending in this application. Claims 11 and 12 have been canceled by a previous amendment.

### *Priority*

**3.** Acknowledgment is made of applicants' claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed with this application.

### *Drawings*

**4.** The drawings filed on 2/10/2005 are objected to by the examiner. Figures 2 and 3 are not legible. Replacement drawings are requested.

### *Sequence Compliance*

**5.** This application contains sequences in the specification which does not comply to 37 CFR 1.821 (d) for failing to reference to the sequences by use of sequence identifiers, preceded by " SEQ ID NO" in the text of description. See for example page 19, lines 14 and 16. These nucleotides should be identified by SEQ ID NO: A corrected sequence listing and new CRF in compliance with sequences rules are required. Appropriate corrections are required.

### *Information Disclosure Statement*

**6.** The information disclosure statement filed 2/10/2005 has been considered. An initialed copy is enclosed.

### *Specification*

**7.** The disclosure is objected to because of the following informalities:

The use of the trademarks Carbopol, Star etc have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

The disclosure is objected to because it contains embedded hyperlink and/or other form of browser-executable code. (see pages 3, 7 and 11) Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Specification page 22 contains a large blank space. Clarification is requested.

Appropriate corrections are required.

***Election/Restrictions***

**8.** Applicants' election with traverse of 7/20/2007 is acknowledged. Applicants elected group II (claims 7-10) drawn to a protein. The traversal is on the ground(s) that the restriction between inventions II (claims 7-10) and invention III (claims 13-18) should be withdrawn. This is not found persuasive because the inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature-linking groups I-V appears to a nucleic acid sequence encoding a 22.5 kD *Streptococcus uberis* protein. However, Jayarao et al. (Journal of Clinical Microbiology, Vol. 30, No. 5, pp. 1347-1350, May 1992) teach total DNA sequence of *Streptococcus uberis* encoding numerous proteins from (see abstract, page 1347 and). Jayarao et al. teach total DNA or genomic sequence of *Streptococcus • uberis* (see abstract). Since applicants' SEQ ID NO: 1 is also a DNA sequence of *Streptococcus uberis.* Therefore, the nucleic acid sequence encoding a 22.5 kD *Streptococcus uberis* protein will be inherent in the DNA and proteins taught by Jayarao et al. Therefore, the technical feature linking the inventions of groups I-V does not constitute a special technical feature as defined by the PCTRule 13.2, as it does not define a contribution over the prior art. As set forth above, each of group I-V has a special technical feature that is not required for the other groups.

The requirement is still deemed proper and is therefore made FINAL.

As to election of species the applicants elected species of claim 7 at least 93% homology. Upon further consideration the office withdraws election of species to %

homology therefore claims 7-10 are under consideration. Claims 1-6 and 13-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions.

***Claim Objections***

**9.** Claim 10 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim, depending from claims 7-9. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

***Claim Rejections - 35 USC § 101***

**10.** 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

**11.** Claims 7 - 9 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 7 and 9 are drawn to a protein that could find in nature. The claimed invention is drawn to a product of nature. Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process. Diamond v. Chakrabarty. 206 USPQ 193 (1980). Additionally, purity of naturally occurring product does not necessarily import patentability. Exparte Siddiqui 156 USPQ 426 (1966). However when purity results in new utility, patentability is considered. Merck Co. V. Chase Chemical Co. 273 F. supp 68 (1967). See also American Wood v. Fiber Disintegrating Co, 90 U5 566 (1974): American Fruit Growers v. Brogdex Co 283 U5 1 (1931). Funk brothers seed Co. V. Kalo Innoculant Co. 33 U5 127 (1948). Filing of arguments and evidence of a new utility imparted by the increased purity of the claimed invention and amendment to the claims to recite the essential purity of the claimed products is suggested to obviate the rejection. For example. "An isolated product..."

***Claim Rejections - 35 USC § 112***

**12.** The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**13.** Claim 7- 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 7 - 9 recite a group of immunogenic protein and fragments thereof. With respect to % identity or numbers of substitutions/deletions/additions where said immunogenic fragment has a sequence homology of at least 93%, 94%, preferably 95% and more preferably 96% to SEQ ID NO: 2. The specification recites "Again another embodiment of the present invention relates to the use of a 22.5 kD *Streptococcus uberis* protein, or an immunogenic fragment of that protein having a length of at least 6 amino acids, wherein that protein or immunogenic fragment thereof has an amino acid sequence homology of at least 70%, preferably 80%, more preferably 85% with the amino acid sequence as depicted in SEQ ID NO: 2 for the manufacturing of a vaccine for combating *Streptococcus uberis* infection. Even more preferred is a sequence homology of 90%, 95%, 97%, 98%, 99% or even 100% in that order of preference (see page 9)." The specification and the claims do not indicate what distinguishing attribute are shared by the members of the genus. Thus the scope of the claims include numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify the members of the genus, and because the genus is highly variant, just naming the proteins is insufficient to describe the genus and derivatives thereof. Thus applicant has not described a function, which is shared by the full length or derivative thereof,

which would adequately describe the genus. One skilled in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Since the specification gives no guidance on or exemplification of how to anticipate the specific homologues, analogues or derivatives thereof, having variant amino acid sequences from claimed proteins. Substitution of amino acids into a known sequence as well as identifying and using fragments of proteins containing an isolated functional domain of a protein is within the realm of protein chemistry and is one of the most unpredictable areas of protein chemistry. For example Burgess et al. (J of Cell Biology, 1990 Vol. 111, pp.2129-2138) teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Furthermore, Lazar et al (Molecular and Cellular Biology, 1988, Vol. 8, pp. 1247-1252) teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. *Streptococcus uberis* genom DNA and its proteins are known in the art for example see Jayarao et al and Leigh et al. (Proir art of recode) However, these references are silent about variant amino acid sequences from these claimed proteins.

The Guidelines for the Examination of Patent Application Under 35 U.S.C. 112, 1st paragraph "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in the position of the genus ( Federal Register, Vol.

66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Since the disclosure fails to describe the common attributes or characteristics that identify the members of the genus, and because the genus is highly variant, SEQ ID NO: 2 is insufficient to describe the genus of % homology variants or fragments thereof. Adequate written description requires more than a mere statement that is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. LTS*. 18 USPQ 2d 1016. Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Application Under 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 64, No.244, pages 71427-71440, Tuesday December 21, 1999.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain,

species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus...."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

***Claim Rejections - 35 USC § 102***

**14.** (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**15.** Claims 7 - 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Leigh et al. (vaccine, vol. 17, pp. 851-857, 1999).

The claims are drawn to a 22.5 kD *Streptococcus uberis* immunogenic protein. Leigh et al. teach *Streptococcus uberis* immunogenic proteins as vaccine antigens ranging from 20 kD to 66 kD. Leigh et al. do not explicitly teach fragments which has a sequence having at least 93%, 94%, preferably 95% and more preferably 96% homology to SEQ ID 2. These fragments will be inherent in the proteins taught by Leigh et al.

***Status of the Claims***

**16.** No claims are allowed.

Claims 7-9 are rejected.

Claim 10 is objected to.

Claims 1-6 and 13-20 are withdrawn from further consideration as being drawn to non-elected inventions.

***Conclusion***

**17.** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (571)-272-0863. The examiner can normally be reached on Mondays and Wednesdays from 12:30-6:30 PM and Thursdays from 12:30-4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew can be reached on 571-272-0787.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Khatol Shahnan-Shah . B.S.,
Pharm, M.S.
Biotechnology Patent Examiner
Art Unit 1645
September 26, 2007

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER